Severe acute respiratory syndrome coronavirus 2 vaccines: The good, the bad, and the ugly

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Abstract

The coronavirus disease pandemic is caused by the highly infectious severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The infection can result in mild-to-severe disease, although many asymptomatic infections are described. There are many types of vaccines with different characteristics, and many have reached Phase III of clinical trials. In this review, we included the main vaccines approved worldwide, including those approved in Mexico. Vaccine-induced immune thrombotic thrombocytopenia has been described, especially in adenovirus vector vaccines. There are specific concerns around vaccine safety and efficacy in special populations such as pregnant women and immunosuppressed individuals. Even though the evidence is scarce, vaccine application remains recommended in most cases. We concluded that the risks of adverse effects from the vaccines are minimal compared to the current risk of contracting the SARS-CoV-2 infection. The benefit of applying the vaccines is greater than not applying them at all.

Key words: Coronavirus disease. Vaccines. Vaccine development.

Introduction

At the end of 2019, a novel coronavirus now known as severe acute respiratory syndrome coronavirus (SARS-CoV-2) was identified as the cause of a cluster of pneumonia cases in Wuhan, a city in China's Hubei Province. It rapidly spread, resulting in a global pandemic. SARS-CoV-2 is now the leading cause of severe acute respiratory syndrome. As of May 2021, it has caused more than 154 million cases and over 3 million deaths worldwide¹.

The dramatic increase in the virus spread, as well as raising the mortality rate of coronavirus disease (COVID-19) around the world, has led many

researchers toward finding potential vaccine candidates for protection against SARS-CoV-2. An efficacious vaccine is essential to prevent further morbidity and mortality. Therefore, vaccine immunity has become a major public health challenge for governments, physicians, and scientists worldwide.

Vaccines against COVID-19 were an essential global intervention to control the current pandemic situation. Vaccines often cause adverse events; however, the vast majority of adverse events following immunization are a consequence of the vaccine stimulating a protective immune response and not allergic in etiology.

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Overview of vaccine development

The development of pharmaceuticals, vaccine development progresses through preclinical evaluation and three distinct clinical stages²:

Preclinical testing

Scientists test a new vaccine on cells and then give it to animals such as mice or monkeys to see if it produces an immune response.

Phase I trials: These are designed to test vaccine safety, although immunogenicity is also measured; dose-ranging studies are also often included.

Phase II trials: These expand the safety profile and immune response assessment in a larger number of participants.

Phase III trials: These are designed to determine efficacy in preventing a predefined endpoint, usually laboratory-confirmed disease. The vaccine efficacy percentage is the reduction in disease incidence among those who received vaccination versus those who received the control product. Efficacy criteria for SARS-CoV-2 trials are discussed elsewhere.

Conventionally, these steps occur sequentially, and each usually takes several years to complete. COVID-19 vaccine development has been accelerated, with each step occurring over several months. In addition, in the COVID-19 vaccine initiative, Phase I and II and Phase II and III studies have frequently been combined with a seamless transition from one phase into the next. At this moment, some vaccines are still in Phase III trials, such as Cansino, Sinovac, Gamaleya, Bharat Biotech, and their final Phase III results have not been published in any journal. However, some preliminary data have been published in their official press release (Table 1)³⁻¹¹.

Vaccine-induced immune thrombotic thrombocytopenia (VITT)

By the end of February, a thrombotic syndrome was observed in a small number of individuals who received the ChAdOx1 CoV-19 vaccine (AstraZeneca, University of Oxford, and Serum Institute of India), an adenoviral vector-based vaccine¹². Afterward, similar findings were observed in a small number of individuals who received the Ad26.COV2.S vaccine (Janssen; Johnson and Johnson), also based on an adenoviral vector¹³. This syndrome has been designated VITT. It has also been called thrombosis with thrombocytopenia syndrome and vaccine-induced prothrombotic immune thrombocytopenia.

Current vaccine recommendations for special populations

ALLERGY AND ANAPHYLAXIS

Contraindications to COVID-19 vaccination are severe or immediate allergic reactions to the vaccine or any of its components. All individuals should be monitored for an immediate reaction following vaccination. Individuals without a contraindication who have a history of anaphylaxis of any kind, an immediate allergic reaction to other vaccines or injectable therapies, or a contraindication to a COVID-19 vaccine class other than the one they are receiving should be monitored for 30 min. All other individuals are monitored for 15 min.

PREGNANT WOMEN

None of the vaccines listed in this review contain a virus that replicates; thus, they do not cause disease, but non-specific side effects from immune response activation may occur. Based on how mRNA and viral vector vaccines work, experts believe they are unlikely to pose a risk for pregnant persons, the fetus, or breastfeeding newborns¹⁴. It is advised for pregnant individuals to undergo COVID-19 vaccination as soon as it is available in their countries and avoid deferring until the end of pregnancy. Patients who are at higher risk of exposure to SARS-CoV-2 or at the highest risk of having the severe disease if infected (e.g. patients with diabetes, obesity, or heart disease) may benefit most. Data about the efficacy and safety of COVID vaccines in pregnant individuals are limited, but studies are underway¹⁵.

IMMUNOSUPPRESSION

Eligible individuals who have an immunocompromising condition or are taking immunosuppressive agents should undergo COVID-19 vaccination. Although the immunogenicity and efficacy of the vaccines are uncertain in such individuals and may be lower than those observed in the general population, the potential for severe COVID-19 in this population likely outweighs the uncertainties^{16,17}.

IMMUNE RESPONSE IN COVID PATIENTS

Individuals with a history of SARS-CoV-2 infection should still receive one of these vaccines. Individuals

Table 1. Available vaccines for severe acute respiratory syndrome coronavirus 2 in 2021

Name	Company	Platform	Doses and intended interval	Efficacy against symptomatic COVID-19:	Common side effects:	Rare adverse effects:	Country of origin:	Approved in Mexico:
BNT162b2	Pfizer/BioNTech	mRNA	2 doses, 3 weeks apart	95% ³	-Local injection site reactions -Systemic symptoms (fever, chills, fatigue, myalgias, headache)	Anaphylaxis	Germany, EUA	✓
mRNA-1273	Moderna	mRNA	2 doses 4 weeks apart	94.5% ⁴	-Local injection site reactions -Systemic symptoms (fever, chills, fatigue, myalgias, headache)	Anaphylaxis	USA	
ChAdOx1nCoV-19/AZD1222	AstraZeneca/University of Oxford/Serum Institute of India	Replication-incompetent chimpanzee adenovirus vector	2 doses: 4-12 weeks apart. (Manufacturer recommendation) -8-12 weeks apart. (WHO recommendation)	82.4% ⁵	-Local injection site reactions -Systemic symptoms (fever, chills, fatigue, myalgias, headache)	Very rare thrombotic complications associated with thrombocytopenia: -Cerebral venous sinus thrombosis. -Splanchnic vein thrombosis	United Kingdom	✓
NVX-CoV2373	Novavax	Recombinant protein	2 doses 3 weeks apart	95.6% ⁶	-Local injection site reactions -Systemic symptoms (fever, chills, fatigue, myalgias, headache)	Unknown	USA	
Ad26.COV2.S	Johnson and Johnson	Replication-incompetent adenovirus 26 vector	1 dose	72% ⁷	-Local injection site reactions -Systemic symptoms (fever, chills, fatigue, myalgias, headache)	Very rare thrombotic complications associated with thrombocytopenia: -Cerebral venous sinus thrombosis.	USA	✓
Convidecia	CanSino biologics	Recombinant adenovirus vector	1 dose	65.28% ⁸	Unknown	Unknown	China	✓
CoronaVac	Sinovac	Inactivated virus	2 doses 2 weeks apart	91.25% ⁹	-Local injection site reactions Systemic symptoms (headache, fatigue, myalgia)	-Muscle spasms, eyelid edema, hyposmia	China	✓
Sputnik V	Gamaleya Institute	Recombinant adenovirus Ad26, Ad5	2 doses 3 weeks apart	91.6% ¹⁰	Unknown	Unknown	Russia	✓
Covaxin	Bharat Biotech	Inactivated virus	2 doses 4 weeks apart	78% ¹¹	Unknown	Unknown	India	✓

with recent, documented SARS-CoV-2 infection (including those diagnosed following the first vaccine dose) should have recovered from acute infection and met the criteria for discontinuation of isolation precautions before receiving the vaccine.

CD8 T lymphocytes are critical for destroying virus-infected cells; their amount in peripheral blood is related to asymptomatic to mild and severe COVID-19 disease. It was recently published that SARS-CoV-2 specific T lymphocytes play an important role in long-lasting protection and deserve further investigation after different vaccine applications¹⁸.

There is scientific evidence demonstrating that a single mRNA vaccine to individuals recovered from COVID-19 induces a robust anti-viral antibody response. However, antibody titer was no further increased after a second vaccination, showing that in recovered COVID-19 patients, one single mRNA vaccine boosts high neutralizing antibody titer and memory B cells¹⁹.

Conclusion

Vaccine development, approval, and production have been accelerated to fight the COVID pandemic. Most of the available vaccines have not finished their Phase III trials but have been approved for emergency use. Nevertheless, the preliminary results indicate that all vaccines are safe, and we recommend the public not to hesitate or avoid any of the approved vaccines in their country. The current risks of adverse effects from the vaccines are minimum compared to the current risk of contracting the SARS-COV2 infection. Undesirable effects vary from local pain and skin rash to hyperthermia, irritation, and weakness. Still, all these are transitory and disappear in a day or 2 after inoculation with or without nonsteroidal anti-inflammatory drugs. Religious, philosophical prejudices, and misinformation in social media contribute to resistance to vaccination, but it is clear that benefits are by far superior to minor undesirable side effects²⁰.

Even though it is important to remark the adverse reaction of prothrombotic syndrome observed in individuals who have received the ChAdOx1 CoV-2 vaccine (AstraZeneca, University of Oxford, and Serum Institute of India) and the Ad26.COV2., S vaccine (Janssen; Johnson and Johnson) would be worth the effort to do screening on a population that these reactions may develop and eventually choose which vaccine has a lower probability to cause these side effects. We consider, as mentioned before that the benefit of applying the vaccines is greater than not applying them at all. The economic impact of vaccination in all countries

demonstrated through the years its utility. Therefore, there is not a bad or ugly vaccine.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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